

In the Specification:

Please amend the specification as shown:

Please delete the paragraph on page 4, paragraph [0016] and replace it with the following paragraph:

Figure 1 aligns the amino acid sequences of DtxR (SEQ ID NO: 8), IdeR (SEQ ID NO: 7) and SirR (SEQ ID NO: 9).

Please delete the paragraph on page 5, paragraph [0017] and replace it with the following paragraph:

Figure 2 aligns amino acid sequences of various IdeR/SirR Homologues found in various species of mycobacterium (SEQ ID NOS: 10-13, respectively, in order of appearance).

Please delete the paragraph on page 5, paragraph [0018] and replace it with the following paragraph:

Figure 3 aligns and compares the amino acid sequence of various homologues of various DtxR type repressors, including DtxR from *Brevibacterium lactofermentum* (Bl) (SEQ ID NO: 14), DtxR from *Corynebacterium diphtheriae* (Cd) (SEQ ID NO: 15), IdeR from *Mycobacterium tuberculosis* (Mt) (SEQ ID NO: 16), *M. leprae* [P] (SEQ ID NO: 18), *M. smegmatis* [P] (SEQ ID NO: 17); DesR from *Streptomyces lividans* (Sl) (SEQ ID NO: 19), *M. tuberculosis* SirR, *Staphylococcus aureus* (Sa) SirR (SEQ ID NO: 21), *S. epidermidis* SirR (SEQ ID NO: 20), *Enterococcus faecalis* DtxR homologue [P] (SEQ ID NO: 22). The DtxR homologues from the *Streptococcus gordonii* (SEQ ID NO: 23), *S. mutans* (SEQ ID NO: 24), *S. pneumoniae* (SEQ ID NO: 25) and *S. pyogenes* (SEQ ID NO: 26). The consensus amino acid sequences between these members of the DtxR family of iron-dependent repressors is indicated. *, metal ion coordination residues in the Primary site; #,

metal ion coordination residues in the Ancillary site; @, the single amino acid residue that interacts with a base in the binding of DtxR dimers to the *tox* operator. AMS has clones of *M. tuberculosis* IdeR, *S. aureus* and *S. epidermidis* SirR, and DtxR homologues from *Enterococcus faecalis*, *S. mutans*, *S. pneumoniae*, and *K. pneumoniae*.

Please delete the paragraph on page 4, paragraph [0022] and replace it with the following paragraph:

Figure 7: Alignment of the "iron box" consensus sequence, known DtxR binding sites, and putative *M.tuberculosis* DtxR/IdeR binding sites identified by an *in silico* genome search. The "consensus sequence" at the top of the figure (**SEQ ID NO: 27**) represents the compilation of the 9 aligned sequences in the figure (**SEQ ID NOS: 28-36, respectively, in order of appearance**). The "published consensus" is drawn from the literature. Gene homologues of the downstream ORFs are shown on the right.

Please delete the paragraph on page 15, paragraph [0048] and replace it with the following paragraph:

Mutants of DtxR are generated in accordance with standard techniques. Polymerase chain reaction (PCR) mutagenesis of the *dtxR* gene is described in Vartanian *et al.* [Vartanian, J.-P., Henry, S., & Wain-Hobson, S. (1996) Hypermutagenic PCR involving all four transitions and a sizeable proportion of transversions. *Nucleic Acid Res.*, 24, 2627-2631]. Briefly, *Bgl*II-tagged primers 1515 (5'-ACCAGATCTGCCGAAAACTTCGA-3') (**SEQ ID NO: 1**) and 1516 (5'-ACCAGATCTCCGCCTTTAGTATTTA-3') (**SEQ ID NO: 2**) were used to PCR amplify *dtxR* from plasmid pRDA which carries the wild type *dtxR* operon. The products of the amplification were then digested with *Bgl*II and ligated either into *Bgl*II-linearized pSC6M1 and transformed into *E. coli* TOP10/λRS65T, or ligated into *Bam*HI digested pBR322 and transformed into *E. coli* TOP10/λRS65T/pSC6. Iron-independent mutants of DtxR were then selected on LB agar plates supplemented with Cm and DP in accordance with the procedure described in Sun, *et al.*

Please delete the paragraph on page 15, paragraph [0049] and replace it with the following paragraph:

Broadly speaking, these mutations should conserve the structural integrity and maintain the ability of the repressor to bind and repress gene expression through the consensus or near consensus *tox* P/O sites. Bacterial clones containing mutagenized *dtxR* can be analysed by DNA sequencing and used in functional biochemical assays such as electrophoretic mobility shift assay, native gel analysis and glutaraldehyde crosslinking studies to reveal the activated state of the repressor in question under metal limiting conditions. This can be determined through gel shift analysis or by functional assays, but it is preferably made using the one-step method described by Frigg, *et al.* [Sun, L., vanderSpek, J. & Murphy, J. R. (1998) *Proc. Natl. Acad. Sci. USA*, 95, 14985-14990]. For gel shift analysis the native *tox* operator (*i.e.*, 5'-ATAATTAGGATAGCTTTACCTAATTAT-3') **(SEQ ID NO: 3)** is a 27 base pair interrupted palindromic sequence upstream of the diphtheria *tox* structural gene can be used as a probe. This sequence features a 9-base pair inverted repeat sequence that is separated by 9 base pairs. See Kaczorek *et al.*, *Science* 221:855-858 (1983); Greenfield *et al.*, *Proc. Natl. Acad. Sci. USA* 80:6853-6857 (1983); Ratti *et al.*, *Nucleic Acids Res.* 11:6589-6595 (1983); and Fourel *et al.*, *Infect. Immunol.* 57:3221-3225 (1989). It overlaps both the -10 region of the *tox* promoter and the transcriptional start sites at -45, -40 and -39 upstream of the diphtheria toxin structural gene. See Boyd *et al.*, *J. Bacteriol.* 170:5940-5952 (1988). The minimal essential DNA target site, *i.e.*, 5'-GTAGGTTAGGCTAACCTAT-3' **(SEQ ID NO: 4)**, is a 19 base pair sequence that forms a perfect palindrome around a central C or G -- is described in Tao and Murphy, *Proc. Natl. Acad. Sci. USA* 91:9646-9650 (1994). Additional probes are variants of ToxO based on the *DtxR* consensus-binding sequence (5'- ANANTTAGGNTAGNCTANNCTNNNN-3') **(SEQ ID NO: 5)**. Variants are defined by the following sequence: 5'-TWAGGTTAGSCTAACCTWA-3' **(SEQ ID NO: 6)**. Thus the function of the repressor and mutant can be defined by recognition and binding or regulation of gene expression via the sequences or variants described above.